Vessel Wall Changes In Patients With Systemic Lupus Erythematosus Compared To Controls: A Preliminary MR Imaging Study In Carotid Artery

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Introduction: Systemic lupus erythematosus (SLE) is associated with an increased prevalence of subclinical atherosclerosis and cardiovascular events.[1,2] Carotid plaque is prevalent in 20-30% of SLE patients under age 35 and in up to 100% of those over age 65.[3] It is important for clinicians to detect carotid atherosclerosis in their earliest stages of development, which can give them guidance to implement appropriate preventive and therapeutic procedures. In this preliminary study, we sought to use MR imaging to examine any early abnormalities in fine structures of carotid vessel wall in patients with SLE by comparing them to age- and sex-matched controls.

Methods: *Patients:* We evaluated bilateral carotid arteries of 43 SLE subjects (39 female, 4 male, mean±SD age 38.05±9.07ys) and 18 controls (17 female,1 male, mean±SD age=38.11±5.97y). Inclusion criteria were:1) age 20-50yrs, disease duration>5years, met the ACR Classification Criteria for SLE; 2) control group was age and sex matched, without heart disease and inflammatory diseases. *MRI protocol:* 3T clinical scanner (Achieva 3T, Philips Medical Systems, Best, Netherlands) with black-blood vessel wall imaging including non-contrast T1-, T2- and proton-density-weighted sequences as well as a T1-weighted dynamic contrast-enhanced sequence (only 28 SLE subjects and 12 controls had contrast injection) was used(Figure 1). Low dose Gd-DTPA (0.05mmol/kg) was injected, followed by a repeat post-contrast T1-weighted sequence. *Image analysis:* CASCADE software package was used to detect[6]: 1) any focal or diffuse wall thickening in the segment (3.2 cm) around carotid bifurcation; and 2) vessel wall enhancement in the common carotid artery. Per-slice measurements from control subjects were used to establish the 95% upper limits of maximum wall thickness and maximum-to-minimum wall thickness ratio for each of the three sub-segments (common carotid, carotid bulb, internal carotid), which were subsequently used as reference to define wall thickening in all subjects. Percent wall enhancement at a given time point (180 seconds after contrast injection) was calculated using signal intensity measurements on post-and pre-contrast images.

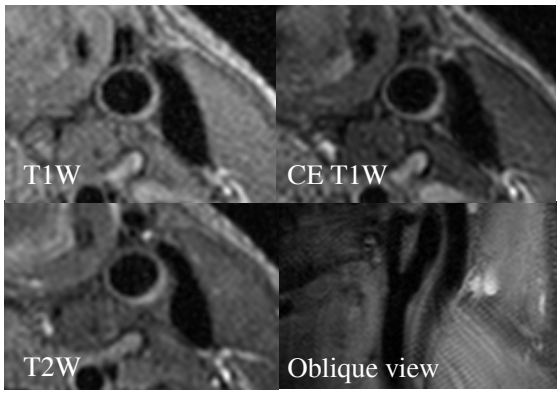

Figure 1.Left CCA (near bulb) in a 33.8 years old female SLE patient, with max wall thickness 0.91mm and mean wall thickness 0.75mm, both were within normal range. While the max/min wall ratio was 1.60, with a ratio in adjacent slice 1.54, two continuous slices met our criterion for wall thickening in CCA. We defined this artery as a slight thickening in left CCA.

Results: We collected bilateral carotid arteries in each subject and statistical analysis were slice based. Criteria for the thickening were based on the 95% upper limits of the normal controls(Table 1). Each artery with 2 continuous slices met any of the criteria was defined thickening of the artery. Any wall thickening (in common carotid, carotid bulb or internal carotid; in left or right carotid) defined using segment-specific thresholds of absolute wall thickness or wall thickness ratio was found in 18 (41.9%) subjects with SLE compared to 2 (11.1%) in the control group (p=0.02). Compared with controls, SLE patients were found to have a significantly higher BMI(P=0.008), Cholesterol (P=0.004), Triglycerides (P=0.028),and Low-density lipoprotein (P=0.035). Disease duration, BMI and C reactive protein did not differ significantly within the SLE group. In the subset of study sample with contrast injection, substantial wall enhancement was observed in subjects with SLE but not in controls (p=0.012).

Segment features	95% upper limits
CCA MaxWT, mm	0.98
CCA Max/Min Ratio	1.39
Bulb MaxWT, mm	1.07
Bulb Max/Min Ratio	1.58
ICA MaxWT, mm	0.92
ICA Max/Min Ratio	1.42

Table 1. 95% upper limits of the volunteer group(N=18).

Characteristic	Patients (N=43)	Controls(N=18)	P value
Age (yr)	38.05±9.07	38.11±5.97	0.978
Female percentage	39(90.70%)	16(88.89%)	0.828
Hypertension (%)	12(27.91%)	1(5.56%)	0.052
Body-mass index(kg/m^2)	23.35±2.36	21.70±1.43	**0.008**
Diabetes (%)	7(16.28%)	0	0.069
TC(Cholesterol, mmol/L)	5.48±1.13	4.62±0.74	**0.004**
TG(Triglycerides, mmol/L)	1.68±0.68	1.26±0.62	**0.028**
HDL (High-density lipoprotein, mmol/L)	1.48±0.49	1.63±0.49	0.292
LDL (Low-density lipoprotein, mmol/L)	3.53±1.18	2.85±1.01	**0.035**
Thicken/Plaque (%)	N=18(25 arteries),41.86%	N=2(2 arteries),11.11%	**0.020**
Features of carotid arteries			
CCA Max wall thickness (mm)	0.82±0.11	0.83±0.08	0.187
CCA Max/Min ratio	1.24±0.15	1.22±0.10	0.110
Bulb Max wall thickness (mm)	0.93±0.12	0.91±0.11	0.460
Bulb Max/Min ratio	1.41±0.22	1.34±0.15	**0.028**

Table 2. Characteristics of Patients with Systemic Lupus Erythematosus and Control Subjects.

Discussion: In SLE group, patients presented a higher prevalence of wall thickening and wall enhancement in carotid artery than volunteer group. Lower HLD, higher ApoA and ApoB100, higher score of SLAM and SLEDAI were associated with premature atherosclerosis in SLE group. Both traditional factors and disease related factors contribute to the atherosclerosis In SLE patients. Dyslipidemia and disease activity were proved to be the most important factors in our study. The higher wall enhancement in SLE patients demonstrated an abnormal wall permeability.

Conclusion: This was one of the first study using MR to evaluate the subclinical atherosclerosis in SLE patients. It represents one of the first attempts that use novel cardiovascular imaging approaches to understand the pathological basis of increased cardiovascular risk in patients with SLE.

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